Department of Veterans Affairs
Tuscaloosa VA Medical Center

Human Research Protection Program SOP #1 **September 28, 2009**

HUMAN RESEARCH PROTECTION PROGRAM (HRPP)

1. POLICY

The Tuscaloosa VA Medical Center (TVAMC) Human Research Protection Program (HRPP) program is committed to its mission of fostering a research environment that promotes respect for the rights and welfare of individuals recruited for, or participating in, research conducted by or under the auspices of the TVAMC.

It is the policy of the TVAMC to ensure the compliance with all VA policies as well as all federal, state, and local laws and regulations. As outlined in this Standard Operating Procedures (SOP), the TVAMC has a systematic and comprehensive HRPP with the qualified and appropriate leadership. All research conducted at the TVAMC involving human participation and/or clinical investigations of FDA-regulated test articles are subject to the TVAMC HRPP policies and procedures.

This SOP establishes that TVAMC research will be carried out in an ethical manner. The basic ethical principles guiding research involving human subjects are provided in the Nuremberg Code, the Declaration of Helsinki, and the Belmont Report. Three basic principles contained in The Belmont Report are central to the ethics of research involving human research and guide the IRB in assuring that the rights and welfare of subjects are protected. Briefly, these three principals are:

- **Respect for Persons**. Individuals should be treated as autonomous agents, and persons with diminished autonomy are entitled to protection (e.g. consent, privacy, and confidentiality).
- **Beneficence**. Research should always be conducted to maximize possible benefits and minimize possible risks to the persons involved.
- **Justice**. There should be equitable selection of subjects, which includes consideration of the following: purposes and setting of the research, the scientific and ethical justification for including vulnerable populations or for excluding classes of persons who might benefit from the research.

The TVAMC will abide by VHA and other Federal requirements for specific protections for human subjects. These applicable laws that govern the TVAMC HRPP include:

- The Federal Policy (Common Rule) for the protection of human subjects ([38 CFR 16] and DHHS Subpart A of the DHHS regulations at [45 CRF 46]).
- 38 CFR 17.33 (provides regulations for human subjects), 38 CFR 17.45 (addresses medical hospital care in research studies), 38 CFR 17.92 (addresses outpatient care for

research studies).
- Food and Drug Administration (FDA) regulations 21 CFR 50 (informed consent regulations), 50 Subpart D (safeguards for children, 56 (IRB regulations), and 312 (investigational new drug application – IND).

2. RESPONSIBILITIES

The TVAMC HRPP is an integrated program that comprises institutional officials, R&D leadership, the Institutional Review Board (IRB), a Research Compliance Officer (RCO), investigators, monitoring bodies, and participants involved in research. HRPP functions are distributed among these groups and the overall organizational structure for protecting research participants is outlined in the TVAMC HRPP Organizational Chart, accompanying SOPs, and Center Memorandums (CM). The HRPP is responsible for establishing a formal process to monitor, evaluate, and continually improve the protection of human research participants; dedicating sufficient resources; exercising oversight of research protection; educating leadership, investigators and research staff about their ethical responsibility to protect research participants; and, providing a mechanism to intervene in research and to respond directly to concerns of research participants.

The TVAMC Director has ultimate responsibility for ensuring the structure, function, and policies of the HRPP to guarantee the protection of human subjects participating in VA-approved research. Also, the Director ensures the availability of resources sufficient to protect the rights and welfare of research participants, taking into consideration the research activities in which they are asked to participate. The Director is the signatory official for the FWA.

The Chief of R&D (C/R&D) ensures that the HRPP is operational and properly implemented. The TVAMC Director delegates responsibility for the TVAMC HRPP to the C/R&D, who is an official with sufficient standing, authority, and independence to ensure implementation and maintenance of the program.

TVAMC R&D Administrative Officer (R&D AO) assists the C/R&D in ensuring that the HRPP is operational and properly implemented. The R&D AO is also the TVAMC HRPP Research Compliance Officer and serves to oversee HRPP education, quality improvement, and compliance audits. The R&D AO also serves as the R&D fiscal point of contact and the grants and contracts manager, under the direction of the C/R&D. The R&D AO/RCO ensures that the HRPP SOPs governing research are readily available to investigators, research staff, and anyone affiliated with the TVAMC in order to ensure that these individuals are informed about their responsibilities when conducting human research. The R&D AO/RCO is responsible for disseminating new information that may affect the HRPP, including laws, regulations, policies, procedures, and emerging ethical and scientific issues.

The **TVAMC Research Compliance Officer (RCO)** reports directly to the Medical Center Director and is responsible for:
- developing and implementing a Research Compliance Program, including the policy for the auditing program

- conducting a complete audit of each VA-approved human research study, according to the schedule provided by the Office of Research Oversight, or as-needed
- conducting an annual audit of each VA-approved human research study for compliance with the regulations and policies on informed consent
- ensuring that audits of human subjects' studies assess compliance with all applicable laws, statutes, regulations, and policies, including those related to privacy, confidentiality, and information security
- reporting non-compliance, as required, to the TVAMC IRB or directly to the Facility Director
- Providing a performance report at least quarterly to the Director

TVAMC Research and Development (R&D) Committee assures compliance with applicable regulations and protection of the rights of human research subjects. Full responsibilities and procedures of the R&D Committee are detailed in TVAMC CM 11-09.

TVAMC Institutional Review Board (IRB) has the responsibility and authority to approve, require modifications (in order to secure approval), or disapprove all research activities (covered by VHA Handbook, 1200.5) regardless of whether the research is funded or non-funded. The full responsibilities and procedures of the IRB are detailed in, the TVAMC HRPP #2 - 21 and TVAMC CM 11-04.

Investigators (Principal and Co-investigators) are responsible for conducting their research in accordance with all agreements with the IRB. Investigator responsibilities are detailed in TVAMC SOP # 13. All investigators are required to comply with all relevant research-related policies and procedures. All requests to conduct research involving human subjects must be submitted in accordance with the requirements set forth in the TVAMC HRPP SOPs.

The TVAMC Privacy Officer is the authoritative source for privacy within VHA and is responsible for developing and implementing a VHA Privacy Program; developing, issuing, reviewing and coordinating privacy policy for VHA in conjunction with policy efforts by VA; coordinating requirements and monitoring compliance with all Federal privacy law, regulations and guidance within VHA; and issuing direction on VHA privacy policies, practices and activities to the field. Specifically, the TVAMC Privacy Officer is responsible for ensuring the facility's overall compliance with privacy policies and requirements, ensuring the facility has a process to review all IRB-approved VA research for compliance with privacy requirements, reporting incidents regarding protected health information (PHI) to the Privacy Violation Tracking System and participating in the investigation of such incidents, and ensuring all employees are trained on privacy annually.

3. DEFINITIONS

a. **Human Research Protection Program** is a comprehensive system consisting of a variety of individuals and committees for the purpose of ensuring the protection of human subjects participating in research. The objective of this system is to assist the institution in meeting ethical principles and regulatory requirements for the protection of human subjects in research.
b. **Research** is "a systematic investigation, including research development, testing, and

evaluation, designed to develop or contribute to generalizable knowledge".

c. **Human Subject** is "a living individual about whom an investigator (whether professional or student) conducting research obtains 1) data through intervention or interaction with the individual or 2) identifiable private information."
d. **An Investigator** is an individual who is engaged in research and/or conducts a research investigation. A **Principal Investigator** is the person under whose immediate direction research is conducted, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.
e. **Federal-wide Assurance (FWA)** is a written commitment by an institution to protect human subjects participating in research. Under federal regulations, any institution conducting or engaging in federally supported research involving human subjects must obtain an Assurance in accordance with 38 CFR 16.103. Note: all research conducted under VA auspices is considered to be Federally supported.
f. **Institutional Review Board (IRB)** is also referred to as the Human Studies Subcommittee. The IRB is a subcommittee of the R&D Committee. An IRB is a board established in accordance with and for the purposes expressed in the Common Rule [38 CFR 16.102 (g).]

4. PROCEDURES

The TVAMC has a current approved Federal Wide Assurance (FWA #00000900). The TVAMC and the TVAMC IRB are committed to fulfilling and implementing the FWA commitments, regardless of sponsorship or regulatory oversight. The Director of the TVAMC is the official responsible for the FWA. Copies of this assurance are provided to all investigators, IRB members, R&D Committee members, and Research Staff. A separate Federal Wide Assurance (FWA#00001289) has also been approved for the Non-Profit Research Corporation, Tuscaloosa Research and Education Advancement Corporation (TREAC). The TVAMC FWA and TREAC FWA are the documented assurances of compliance to protect research participants and these documents are available to all persons involved in the TVAMC HRPP.

The TVAMC HRPP has and follows written policies and procedures governing research with research participants that are available to investigators , IRB and R&D Committee members and research staff affiliated with the TVAMC. Such procedures are coordinated with the TVAMC Institutional Review Board (IRB) and Research and Development (R&D) Committee. As outlined in the IRB SOP, the TVAMC has and follows written policies and procedures that allow the IRB to function independently of other organizational entities in its role in protecting research participants. Research subject to the TVAMC HRPP does not commence until the research has received all approvals required by the TVAMC and the Principal Investigator has been notified by the C/R&D that research may begin. Required approvals at the TVAMC include approvals by the IRB and R&D Committee. The IRB SOP and R&D CM describe the communication and interaction between these two committees, as well as entities within the organization that are involved in the conduct of human research (i.e. laboratory, pharmacy, radiology, and clinical services).

The TVAMC HRPP has and follows written policies and procedures for the following functions:

- To maintain an independent IRB (SOP#2; CM 11-04)
- To review the proposed research study in regard to design, safety, protection of human research participants, and all other requirements prior to the initiation of the research (SOP#3) and at follow-up intervals not to exceed one year (SOP#6).
- To review the scientific or scholarly validity of a proposed research study (CM 11-09).
- To define and provide a mechanism for expedited review of items or research that meet the requirements for expedited review (SOP#4).
- To determine when studies are exempt from applicable federal, state, and local TVAMC policies and procedures and addressing protection of participants in research exempt from applicable federal regulations (SOP#5).
- To define requirements for informed consent, to determine when studies are allowed to waiver or altered informed consent (SOP#7).
- To address patient recruitment, selection practices, and vulnerable subjects (SOP#8).
- To identify, manage, and minimize individual conflicts of interest of investigators and to recognize and manage institutional conflicts of interest (SOP#9A, SOP#9B).
- To address research privacy and data security requirements (SOP #10).
- To address reporting requirements for adverse events, protocol deviations, modifications, and unanticipated problems involving risks to research participants or others (SOP#11).
- To contribute to the improvement of qualifications/expertise and ensure compliance with continuing education requirements for all investigators, IRB and R&D reviewers and committee members, and research staff. All personnel reviewing, conducting, or supporting human research demonstrate and maintain sufficient knowledge of the ethical principles and federal, state, and local requirements for protecting research participants (SOP#12).
- To address investigators' responsibilities and means to allow investigators to bring forward concerns or suggestions regarding the HRPP, including the IRB review process (SOP #13).
- To address participant outreach (SOP#14)
- To address DNA research (SOP #15)
- To work with sponsors, investigators, research participants, and the IRB to uphold ethical standards and practices in research (SOP#16).
- To monitor, measure and improve HRPP effectiveness, quality, and compliance with organizational policies and procedures and applicable federal, state, and local laws (SOP #17)
- To address allegations and findings of non-compliance with HRPP requirements (SOP#18).
- To address that use of any investigational or unlicensed test article in compliance with all federal, state, or local regulations (Pharmacy SOP & CM on Drug Policy)
- To address and ensure that the handling of investigational or unlicensed test articles meets organizational standards relating to pharmacy, inventory control, and documentation (Pharmacy SOP & CM on Drug Policy).
- To address HRPP number of IRBs, budget, resources, and annual reporting requirements (SOP#19)
- To address modifications to previously approved research (SOP#20)

SOP#21 addresses the Research Compliance program which operates in concert with the IRB to assess, promote and ensure that research at the TVAMC complies with applicable laws, regulations and policies related to human subjects research, through the independent conduct of periodic and "for cause" audits.

The types of research typically covered by the TVAMC HRPP are clinical investigations of the cause, evaluation, assessment, treatment, or outcome of clinical medical and psychiatric illnesses. The categories of participants typically covered by the TVAMC HRPP are adults (any age over 19 years), any race or ethnicity, any gender, and nonprisoners. The TVAMC does not conduct research with children, prisoners, pregnant women (as the focus of the study), fetuses, or neonates. The TVAMC does not conduct Animal research, Emergency Use research or Device research. If future need for research with these populations or Animal research, Emergency Use research or Device research arises, the TVAMC HRPP will develop, write, and follow policies and procedures that meet federal and local requirements prior to such research being allowed or conducted.

The TVAMC HRPP may consult with VA Regional Counsel for guidance about regulatory compliance on issues, such as those regarding:

- Areas in which federal and state law differ relevant to human subject research
- Application of laws other than federal law relevant to human subject research
- Application of laws beyond federal law relevant to human subject research
- Contracts or legal agreements
- Travel request to ensure ethical compliance
- Questions concerning legally authorized representative when an adult is unable to provide consent, when needed, and not otherwise addressed in SOP #7 Research Informed Consent

5. REFERENCES

- 21 CFR 50, 56, 312
- 38 CFR 16.102 (g) and 16.103(a), (b)(1) and (c)
- 38 CFR 17.33, 17.45, 17.92
- 45 CFR 46.103(a), (b)(1) and(c)
- M-3, Part I, 2.02b , 3.01b, 9.03c and 9.07
- VHA Handbook, 1200.5

6. ATTACHMENTS

- TVAMC R&D Center Memorandum
- TVAMC HRPP Organizational Chart
- TVAMC Federal Wide Assurance (FWA #00000900)
- TREAC Federal Wide Assurance (FWA#00001289)

7. RESCISSIONS

Human Research Protection Program SOP #1 dated May 7, 2007.

8. REVIEW DATE

January 1, 2012

Signature on file in R&D Office.
Lori L. Davis, MD
Chief of Research and Development